Title : EFFECTS OF ALCOHOL CONSUMPTION ON THE PHARMACODYNAMICS OF ALFENTANIL

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Moderate to heavy alcohol consumers have an increased barbiturate, volatile anesthetic and opioid requirement during anesthesia.[1-3] The aim of this study was to investigate the effect of alcohol consumption on the pharmacodynamics of alfentanil (Alf).

Methods. After local medical ethics committee approval and informed consent two groups of women, ASA I, undergoing curative surgery for primary breast cancer were studied. Group I consisted of 6 patients (45 ± 9 yr, 66 ± 8 kg), who had an average daily consumption of the equivalent of 2-4 units of alcohol (20-40 g). Group II consisted of 8 patients (46 ± 9 yr, 66 ± 5 kg), who were life-long abstainers or who drank only occasionally (< 6 units per year). Patients whose alcohol consumption in the two weeks before surgery was not typical of that in the last year were excluded from the study. No patient had clinical or biochemical evidence of hepatic dysfunction or a history of other drug abuse. Alf was administered by a computer driven infusion pump (TIAC). Anesthesia was induced with 66% N_2O in O_2 and Alf to an initial target plasma concentration of 350 ng/ml, reached in 2 min. If necessary the target concentration was increased. When consciousness was lost succinylcholine, 1 mg/kg, was given. The trachea was intubated and the target Alf plasma concentration was lowered to 200 ng/ml. If during surgery the patient exhibited signs of inadequate anesthesia, the target plasma concentration was increased by 50-100 ng/ml. Inadequate anesthesia was defined as an increase in systolic blood pressure by more than 15 mm Hg above normal, a heart rate higher than 90 beats/min, other autonomic signs or somatic responses. If the patient did not respond during a 15 min period, the target concentration was lowered by 50-100 ng/ml. In order to identify somatic responses minimal doses of pancuronium were used. Alf infusion was stopped 10 min before the anticipated end of surgery. At the end of surgery N_2O was discontinued. Patients were extubated when their ventilation was adequate without stimulation. If, 10 min after stopping N_2O, ventilation was inadequate naloxone was given. Arterial blood samples for determination of plasma Alf concentrations were taken before any change of the target concentration and 4 min after a new predicted target concentration was achieved. An additional blood sample was taken at extubation. Plasma concentrations were determined by capillary gas chromatography. Plasma concentration-effect data were fitted by logistic regression, where effect was either response or no response to surgical stimuli. A two sample t-test was used for intergroup comparisons. Data are presented as mean ± SD.

Results. The average duration of anesthesia in group I was 151 ± 46 min and in group II 144 ± 26 min. The average total Alf requirement in group I was 3.66 ± 1.23 mcg/kg/min, and 1.87 ± 0.41 mcg/kg/min in group II. This difference was highly significant ($p < 0.005$). The plasma concentration-effect curves for individual patients are shown in fig 1. The average Cp50 (that plasma concentration for which the probability of no response during surgery is 50%) in group I was 522 ± 103 ng/ml. The average Cp50 in group II was 208 ± 26 ng/ml. This difference was highly significant ($p < 0.001$). One patient in group I and two patients in group II needed naloxone to restore spontaneous ventilation. The average plasma concentration at extubation in the patients who did not need naloxone was 372 ± 114 ng/ml in group I and 176 ± 39 ng/ml in group II. This difference was highly significant ($p < 0.005$).

Discussion. In patients with an average daily consumption of 20-40 g alcohol the Cp50 of alfentanil for the surgical procedure was more than double that of non-drinkers. A similar difference was found for the plasma concentration at which ventilation was adequate. Our results suggest that the increased requirement for opioids in patients who are moderate to heavy alcohol drinkers is mainly due to a decreased sensitivity to the central nervous system effects of opioids.

References

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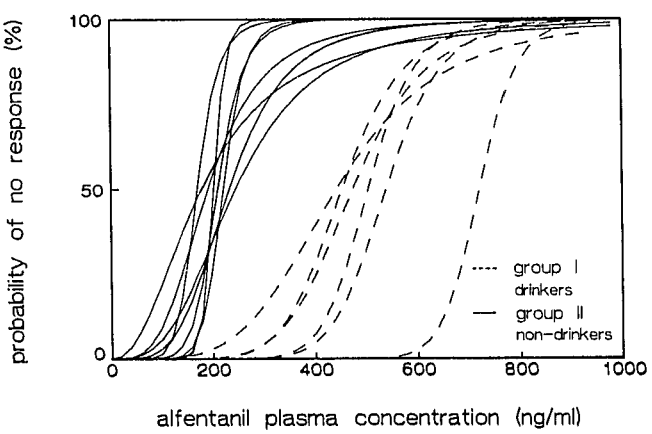

Fig. 1. Alfentanil plasma concentration vs effect curves for individual patients during surgery. The Cp50 and slope of these curves were defined from the quantal responses of the individual patients to the surgical stimuli using logistic regression.